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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,024	08/28/2001	Lance E. Steward	17452 (BOT)	7269

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EXAMINER

SHAHNAN SHAH, KHATOL S

ART UNIT PAPER NUMBER

1645

DATE MAILED: 04/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/942,024	STEWART ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 35-53 is/are pending in the application.
- 4a) Of the above claim(s) 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 35-36 and 38-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicants' amendments and response of 12/19/2003 and 2/3/2004 are acknowledged.

Claims 42 and 49-52 have been amended. Specification pages 4-5 have been amended.

2. Claims 35-53 are pending. Claims 35-36 and 38-53 are under consideration.

Prior Citations of Title 35 Sections

3. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Prior Citations of References

4. The references cited or used as prior art in support of one or more rejections in the instant office action have been previously cited and made of record. No form PTO-892 has been submitted with this office action.

Drawings

5. Objection to the drawings made in paragraph 5 of the office action mailed September 23, 2003 is maintained. Applicants have not submitted corrected drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Objections Withdrawn

6. Objections to the specification made in paragraph 6 of the office action mailed September 23, 2003 have been withdrawn in view of applicants' amendment and response.

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Objections maintained

7. Objections to claims 39-40 made in paragraph 7 of the office action mailed September 23, 2003 are maintained. Withdrawal of claim 37 and removal of that embodiment leaves the claims in improper form (i.e, the method of claim 35, 36). There should be an alternative language recited in the claims (i.e, the method of claim 35 or 36).

Rejections Withdrawn

8. Rejection of claims 49-51 under 35 U.S.C. 112, first paragraph made in paragraph 10 of the office action mailed September 23, 2003 has been withdrawn in view of applicants' amendment and response.

9. Rejections of claim 35-53 made in paragraph 13 of the office action mailed September 23, 2003 have been withdrawn in view of applicants' amendment and response.

Rejections Maintained

10. Rejection of claims 35, 36, 38, 39, 41,42, 44, 45, 47, 48 and 53 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 61, 62, 63, 67, 71, 72, 73, 74, 76, 77, 78, 79, 80, 81, and 82 of copending Application No. 10261161 made in paragraph 9 of the office action mailed September 23, 2003 has been maintained. No terminal disclaimer has been submitted by the applicants.

11. Rejection of claims 35- 36 and 38-53 under 35 U.S.C. 103(a) made in paragraph 15 of the office action mailed September 23, 2003 has been maintained.

The rejection was as stated below:

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Claims 35-36 and 38-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt et al. (US 5,965,699) in view of Clegg (Current Opinion in Biotechnology Vol. 6, pp 103-110, 1995).

Claims are drawn to a method of determining protease activity using fluorescence resonance energy transfer.

Schmidt et al. teach a method of determining protease activity using a labeled based assay (see abstract and claims). Schmidt et al. teach a botulinum toxin substrate and BoNT A peptide sequence (see claim 1). Schmidt et al. also teach BOTOX (see column 12, lines 15-20). Schmidt et al. teach detecting increase or decrease protease activity (see claim 9) and comparing the activity to a control. Schmidt et al. teach using fluorescamine as a fluorophore. Schmidt et al. do not teach FRET. However, Clegg teaches utility of fluorescence resonance energy transfer in biological assays and for study of enzymes (see abstract and page 106 under biotechnological applications).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the method taught by Schmidt et al. with well known FRET method taught by Clegg to obtain the claimed method.

One having ordinary skill in the art would have been motivated by the teachings of Clegg that FRET assays can be exploited for fluorometric enzyme assays. (see page 106 under biotechnological applications) to use FRET assay for determining protease activity of botulinum toxins.

Applicants arguments of 12/19/2003 have been fully considered but they are not persuasive.

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Applicants argue that cited references do not teach the claimed invention and there is no motivation to modify the assay of Schmidt by incorporating FRET.

It is the examiner's position that it seems that the applicants argue the references Individually.

In response to applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicants' argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to modify the assay of Schmidt by incorporating FRET comes from the teaching of Clegg "The benefits of fluorescence resonance energy transfer are becoming increasingly evident to researchers who require measurements with high sensitivity, specificity, noninvasiveness, rapidity and relative simplicity" see abstract. Clegg also teaches "In another study, FRET has been employed to observe the toxic effects of cytolytic toxins (see page 104).

Conclusion

12. No claims are allowed.

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13. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

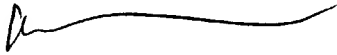
14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol S Shahnian-Shah whose telephone number is (571)-272-0863. The examiner can normally be reached on 7:30am-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith can be reached on (571)-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Khatol Shahnian-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

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April 17, 2004



RODNEY P. SWARTZ, PH.D.
PRIMARY EXAMINER